Specifications

Version	Change control
02	Update analytical scope
03	Update analytical scope + new chapters „Important information regarding the analytical services“

1 Newborn screening

Target disease	Analyte	Method	Sample type	Sample amout	Processing time [1]	Accredited (ISO 15189)
			Total amount:	*5 Spots*		
Congenital Adrenal Hyperplasia	17α-Hydroxyprogesterone Steroid profile *(2nd tier)*	Fluorimetry (SOP 2.3.1) HPLC-MS/MS (SOP 2.3.14)	DBS	2-3 Spots	24 h	yes -
Maple syrup urine disease (MSUD)	(Iso)leucine	MS/MS (SOP 2.3.9)	DBS	2-3 Spots	24 h	yes
Biotinidase deficiency	Biotinidase	Fluorimetry (SOP 2.3.1)	DBS	2-3 Spots	24 h	yes
Carnitine-acylcarnitine translocase deficiency (CACT)	Free carnitine, long-chained acylcarnitines	MS/MS (SOP 2.3.9)	DBS	2-3 Spots	24 h	yes
Carnitine-palmitoyltransferase deficiency type 1 (CPT I)	Free carnitine, long-chained acylcarnitines	MS/MS (SOP 2.3.9)	DBS	2-3 Spots	24 h	yes
Carnitine-palmitoyltransferase deficiency type 2 (CPT II)	Free carnitine, long-chained acylcarnitines	MS/MS (SOP 2.3.9)	DBS	2-3 Spots	24 h	yes
Classical galactosemia	Galactose-1-P-Uridyltransferase Total galactose *(2nd tier)*	Fluorimetry (SOP 2.3.1) Photometry (SOP 2.3.5)	DBS	2-3 Spots	24 h	yes yes
Glutaric aciduria type 1	Glutarylcarnitine	MS/MS (SOP 2.3.9)	DBS	2-3 Spots	24 h	yes
Hypothyroidism	Thyroid-stimulating hormone (TSH)	Fluorimetry (SOP 2.3.1)	DBS	2-3 Spots	24 h	yes
Isovaleric acidemia	C5-carnitine, Isovalerylcarnitine, Pivaloylcarnitine *(2nd tier)*	MS/MS (SOP 2.3.9) HPLC-MS/MS (SOP 2.3.13)	DBS	2-3 Spots	24 h	yes yes
LCHAD- deficiency	Long-chain acylcarnitines	MS/MS (SOP 2.3.9)	DBS	2-3 Spots	24 h	yes
VLCAD- deficiency	(Very) long-chain acylcarnitines	MS/MS (SOP 2.3.9)	DBS	2-3 Spots	24 h	yes
MCAD-deficiency	Medium chain acylcarnitines	MS/MS (SOP 2.3.9)	DBS	2-3 Spots	24 h	yes
Phenylketonuria & hyperphenylalaninemia	Phenylalanine	MS/MS (SOP 2.3.9)	DBS	2-3 Spots	24 h	yes
Cystic fibrosis (CF)	Immunoreactive trypsinogen (IRT) Pancreatitis-associated protein (PAP) CF-genetics (31 mutations)	Fluorimetry (SOP 2.3.1) Fluorimetry (SOP 2.3.7) PCR (SOP 2.3.8)	DBS	2-3 Spots 2-3 Spots 2-3 Spots	24 h 2-14 days 2-14 days	yes yes yes
Severe combined immunodeficiency (SCID)	TREC	PCR (SOP 2.3.10)	DBS	2-3 Spots	24 h	yes
Sickel cell disease (SCD)	Hemoglobin S, C, D, E, O	MS/MS (SOP 2.3.11)	DBS	2-3 Spots	24 h	yes

Spinal muscular atrophy (SMA)	SMN1	qPCR (SOP 2.3.10)	DBS	2-3 Spots	24 h	yes
Tyrosinemia Type I	Succinylacetone	MS/MS (SOP 2.3.9)	DBS	2-3 Spots	24 h	yes

[1] The processing time does not include Sundays and public holidays in Germany. The operation time of the laboratory is from Monday – Friday (8 am – 4 pm) and Saturday (8 – 12 am).

Sample types and container:

DBS – Dried blood spot card

1.1 Important information regarding the analytical services

According to the German Genetic Diagnostics Act and the Children's Guidelines, a declaration of consent from at least one legal guardian is required for newborn screening. A corresponding form is available on our website: https://www.uke.de/kliniken-institute/kliniken/kinder-und-jugendmedizin/für-weisende-ärzte/laborleistungen/

For all diseases included in the newborn screening, variants are known that are not detected by the offered tests. Further diagnostics must be carried out, regardless of the newborn screening result, if a disease is persistently suspected.

The newborn screening results are only valid if no blood product transfusion and no corticosteroide or catecholamine administration have been applied prior to the blood sampling.

The TREC-based newborn screening for severe combined immunodeficiencies (SCID) does not detect certain mild (e.g. ADA gene) or rare forms of SCID (e.g. ORAI1, CARD11, IKBKB, MHC-II deficiency).

The IRT-based newborn screening for cystic fibrosis can produce false negative results in case of meconium ileus. Therefore, further diagnostics for cystic fibrosis (e.g. sweat test) must be carried out in the case of meconium ileus.

The screening for 5q-associated SMA only detects 5q-associated spinal muscular atrophy caused by homozygous deletions of the SMN1 gene, which causes around 95% of severe infantile SMA forms. Compound heterozygous carriers of point mutations of the SMN1 gene are not detected.

2 Selective metabolic diagnostics

Target disease	Analyte	Method	Sample type	Sample amout	Sampling instructions	Processing time [2]	Accredited (ISO 15189)
Lysosomal enzymes			*Total amount:*	*3-5 Spots*			
Pompe disease	α-Glucosidase	Fluorimetry (SOP 2.4.1)	E DBS	1 ml 2-3 Spots		1-2 weeks	yes yes
Gaucher disease	β-Glucosidase	MS/MS (SOP 2.4.3)	E DBS	1 ml 2-3 Spots		1-2 weeks	yes yes
Acid sphingomyelinase deficiency (Before Niemann-Pick A/B disease)	Acid sphingomyelinase	MS/MS (SOP 2.4.3)	E DBS	1 ml 2-3 Spots		1-2 weeks	yes yes
Fabry disease	α-Galactosidase	MS/MS (SOP 2.4.2)	E DBS	1 ml 2-3 Spots		1-2 weeks	yes yes
Mucopolysaccharidosis			*Total amount:*	***3-5 Spots***			
Multiplex (MPS II, IIIB, IVA, IVB, VI, VII) - MPS II - MPS IIIB - MPS IVA - MPS IVB - MPS VI - MPS VII - Mukolipidose II/III	 Iduronat-2-sulfatase N-Acetylglucosaminidase N-Acetylgalactosamin-6-sulfatase β-Galactosidase Arylsulfatase B β-Glucuronidase N-Acetylglucosamin-1-Phosphotransferase	MS/MS (SOP 2.4.8)	E DBS	1 ml 2-3 Spots		2 weeks	yes yes
MPS I	α-Iduronidase	MS/MS (SOP 2.4.5)	E T	5-10 ml 2-3 Spots	**	2 weeks	yes yes
MPS IIIA (Sanfilippo A)	Heparan-N-sulfatase	Fluorimetry (SOP 2.4.18)	E	5-10 ml	**	2 weeks	-
MPS IIIC (Sanfilippo C)	Acetyl CoA: α-Glucosaminid-N-acetyltransferase	Fluorimetry (SOP 2.4.18)	E	5-10 ml	**	2 weeks	-
Neuronal ceroid lipofuscinosis			*Total amount:*	***3-5 Spots***			
Neuronal Ceroid Lipofuscinnoses Type 1 (CLN1)	Palmitoyl protein thioesterase 1	Fluorimetry (SOP 2.4.20)	E DBS	1 ml 2-3 Spots		1-2 weeks	yes yes
CLN2	Tripeptidyl peptidase 1	Fluorimetry (SOP 2.4.20)	E DBS	1 ml 2-3 Spots		1-2 weeks	yes yes
Oligosaccharidosis			*Total amount:*	***3-5 Spots***			
α-Mannosidosis	α-Mannosidase	Fluorimetry (SOP 2.4.12)	E DBS	1 ml 2-3 Spots		1-2 weeks	- -
β-Mannosidosis	β-Mannosidase	Fluorimetry (SOP 2.4.13)	E DBS	1 ml 2-3 Spots		1-2 weeks	- -

α-Fucosidosis	α-Fucosidase	Fluorimetry (SOP 2.4.14)	E DBS	1 ml 2-3 Spots		1-2 weeks	- -
Gangliosidosis			***Total amount:***	***3-5 Spots***			
GM1-Gangliosidosis	β-Galactosidase	Fluorimetry (SOP 2.4.15)	E DBS	1 ml 2-3 Spots		1-2 weeks	- -
GM2-Gangliosidosis	Total hexosaminidase	Fluorimetry (SOP 2.4.9)	E DBS	1 ml 2-3 Spots		1-2 weeks	- -
GM2-Gangliosidosis	Hexosaminidase A	Fluorimetry (SOP 2.4.9)	E DBS	1 ml 2-3 Spots		1-2 weeks	- -
Leukodystrophies			***Total amount:***	***3-5 Spots***			
Metachromatic leukodystrophy	Arylsulfatase A	Fluorimetry (SOP 2.4.17)	E	5-10 ml	**	1-2 weeks	-
Krabbe disease	β-Galactocerebrosidase	MS/MS (SOP 2.4.4)	E DBS	1 ml 2-3 Spots		1-2 weeks	yes yes
Other							
Wolman disease, CESD	Lysosomal acid lipase	Fluorimetry (SOP 2.4.10)	E DBS	1 ml 2-3 Spots		1-2 weeks	yes yes
Other enzymes							
Biotinidase deficiency	Biotinidase	Fluorimetry (SOP 2.3.1) Fluorimetry (SOP 2.3.1) Photometry (SOP 2.4.28)	E DBS P	1 ml 2-3 Spots 1-2 ml	*	2-4 weeks	yes yes -
Galactosemia	Galactose-1-P-Uridyltransferase	Fluorimetry (SOP 2.3.1)	E DBS	1 ml 2-3 Spots		24 h	yes yes
Fatty acid oxidation disorders, organic acids							
Several diseases	Acylcarnitines	MS/MS (SOP 2.3.9)	E DBS P	1 ml 1 Spot 1 ml		24-48 h	yes yes yes
Several diseases	Organic acids	GC/MS (SOP 2.4.29)	U	5-10 ml		1-2 weeks	-
Amino acids							
Several diseases	Amino acids	MS/MS (SOP 2.3.9) MS/MS (SOP 2.3.9) HPLC-MS/MS (SOP 2.4.36) HPLC-MS/MS (SOP 2.4.36)	E DBS P CSF	1 ml 2-3 Spots 1 ml 1 ml	*	24-72 h	yes yes yes -
Several diseases	Amino acids	HPLC-MS/MS (SOP 2.4.36)	U	5-10 ml		2-4 days	-
Diagnosis: Argininosuccinic aciduria	Argininosuccinic acid	MS/MS (SOP 2.3.9)	DBS	2-3 Spots		24 h	yes
Diagnosis / Follow-up:	Succinylacetone	MS/MS (SOP 2.3.9)	DBS	2-3 Spots		24 h	yes

Tyrosinemia Type I							
Follow-up: Phenylketonuria (PKU)	Phenylalanine, Tyrosine	MS/MS (SOP 2.3.9)	DBS	2-3 Spots		24 h	yes
Follow up: MSUD	Leucine, Isoleucine, Valine	MS/MS (SOP 2.3.9) HPLC-MS/MS (SOP 2.4.36)	E P	1 ml 1 ml	* *	24-72 h 24-72 h	yes yes
Fatty acids							
Follow-up of known patients e.g. under dietary treatment	Essential fatty acids	GC/MS (SOP 2.4.22)	P	1-2 ml		2-3 weeks	-
Peroxisomal disorders	Very long-chain fatty acids	GC/MS (SOP 2.4.22)	P	1-2 ml		2-3 weeks	-
Peroxisomal disorders	Phytanic acid	GC/MS (SOP 2.4.22)	P	1-2 ml		2-3 weeks	-
Special diagnostics in urine							
Lysosomal storage diseases (MPS / multiple sulfatase deficiency)	Glycosaminoglycans (GAG)	Photometry (SOP 2.4.30)	U	1-2 ml		2-3 weeks	-
Other special diagnostics							
Sweat test for cystic fibriosis *(internal samples only!)*	Chloride	Titrimetry (SOP 2.4.35)	SW	50 – 100 µl		24 h	-
Several liver diseases	Total bile acids	Photometry (SOP 2.4.24)	S	1 ml		48-72 h	-
Other diagnostics in blood							
Galactokinase deficiency (and other galactosemias)	Total galactose	Photometry (SOP 2.3.5)	E DBS	1 ml 2-3 Spots		24 h	yes yes
Congenital disorders of glycosylation	CDG-diagnostics, Transferrin	Gel electrophoresis (IEF, SOP 2.4.27)	S	1-2 ml		2-3 weeks	-

[2] The processing time does not include weekends and public holidays in Germany. Express analysis can be offered for most diseases. Please contact us in advance for further details. Express samples must arrive before 11 am.

The operation time of the laboratory for selective metabolic diagnostics is from Monday – Friday (8 am – 4 pm)

* cooled shipping required. Please send the centrifugation supernatant only!

** Amongst others, EDTA-blood is required for leukocyte isolation. Please send the EDTA-blood samples uncooled by express mail at the beginning of the week (samples must arrive before Friday, 12 am, not on Saturday).

Sample types and container:

E - Blood collection tube (with EDTA as anticoagulant)

P - Blood collection tube (with anticoagulants like EDTA or heparin)

S - Serum tube (without anticoagulants)

DBS –Dried blood spot card

U – Urine tubes / screw cap container

CSF – Cerebrospinal fluid

SW – Sweat

2.1 Important information regarding the analytical services

For all offered enzyme activity tests, rare atypical disease variants are known that are not detected by these tests. Further diagnostics (e.g. other biochemical or genetic tests) must be carried out, regardless of the enzyme activity test result, if a disease is persistently suspected.